REMARKS

Claims 1-30 are pending in the present application.

The rejections of: (a) Claims 1-8, 12-15, 20-22, 24, 26-28, and 30 under 35 U.S.C. §102(b) over Masunari et al; and (b) Claims 1-9, 12-16, 20-22, 24, 26-28, and 30 under 35 U.S.C. §102(b) over LaFrentz et al, are respectfully traversed.

Applicants submit that the Examiner's rejections over Masunari et al and LaFrentz et al are without merit and overlook a critical element of the claimed invention. Specifically, none of Masunari et al and LaFrentz et al disclose inactivation of a logarithmic growth phase culture.

The rejections over Masunari et al and LaFrentz et al were maintained for the same basic reason. It is the Examiner's position that "logarithmic phase is defined as the phase where binary fission occurs and the rate of increase in cell number is multiplication function of cell number. The culture of [reference] is in logarithmic phase because the cells are increased in cell number and is a multiplication function of the cell number." However, the Examiner offers no support for this conclusion.

Where it is maintained that there is an implicit teaching or suggestion in the prior art, "the Examiner should indicate where (page and line or figure) such a teaching or suggestion appears in the prior art." (*Ex parte* Jones, 62 USPQ2d 1206, 1208 (Bd. Pat. App. & Inter. 2001). However, in the present application the Examiner has not indicated where, if at all, each claim limitation (i.e., the logarithmic phase culture) may be found in the art of record. On the contrary, the Examiner merely provides allegations that this limitation is met. Further, the Examiner has not provided any evidence that such motivation would have existed as of the time of the present invention.

Masunari et al disclose culturing *F. psychorophilum* for 3 to 3.5 days in modified cytophaga broth at 18°C. LaFrentz et al disclose culturing *F. psychorophilum* for 72 hours in TYES at 15°C. Not withstanding the fact that Masunari et al disclose that the amount of live cells before inactivation was 10^6 CFU/ml, Applicants submit that based the similarities in the growth conditions, the growth curve of *F. psychorophilum* shown in Figure 1 of the present application, and the disclosure at page 9, lines 11-15, it is clear that neither Masunari et al, nor LaFrentz et al disclose inactivation of a logarithmic growth phase culture.

Although the Examiner describes a definition of a logarithmic growth phase as increasing in cell number and alleges that the growth conditions in Masunari et al and LaFrentz et al meet this definition , there is no disclosure in the references to show such an increase in cell number during their growth conditions as the Examiner alleges. Indeed, Masunari et al and LaFrentz et al disclose an incubation period for more than 3 days and 72 hours, respectively. Based on the growth conditions reported in these references, Applicants submit that the culture would not be in logarithmic phase as the Examiner alleges, but rather they would be in the stationary phase. It is a well known fact that the stationary phase is a time of significant physiological change and particularly involves the physiological adaptation of cells to survival through periods of little growth. Frequently these physiological changes are manifest in altered physical structure (e.g., membrane) or differences in protein expression profiles.

Moreover, as shown in Example 4 (Table 1 on page 12 of the specification; reproduced below for the Examiner's convenience), vaccines made from a culture in logarithmic phase (i.e., the present invention) have a higher efficacy than those in stationary phase (i.e., Masunari et al and LaFrentz et al).

TABLE 1

Group	Dosage of Challenge (CFU/mL)	Death/ Challenge	Survival Rate (%)
Logarithmic Growth Phase Group	1.7×10^8	39/152	74[a,c]
Stationary Phase Group	1.9×10^8	39/105	63[b]
Control Group	2.2×10^8	82/165	50

a: Significant difference against control group ($p < 0.001$), chi-square test

b: Significant difference against control group ($p < 0.05$)

c: Significant difference against stationary phase group ($p < 0.05$)

In view of the foregoing, Applicants submit that the term "logarithmic phase" sufficiently characterizes and distinguishes the present invention from the disclosures of Masunari et al and LaFrentz et al. Therefore, none of these references can anticipate the claimed invention.

Applicants request withdrawal of these grounds of rejection.

The rejection of Claims 1-8, 12-15, 20-22, 24, 26-28, and 30 under 35 U.S.C. §102(b) over Rahman et al is respectfully traversed.

In maintaining this ground of rejection, the Examiner refers to the section entitled "Culture Conditions in Broth Medium" on page 173 as disclosing harvesting of cells in logarithmic growth phase. Further, on page 176, Rahman et al disclose that "bacteria were isolated from TY broth and an OMF vaccine was prepared as described for the bacteria isolated from agar plates." This OMF vaccine was then injected intramuscularly. Based on the Examiner's interpretation of these sections, the Examiner alleges that the present invention is anticipated. Applicants disagree.

In drawing the foregoing conclusion, the Examiner overlooks a critical element of the claimed invention – that the *Flavobacterium psychrophilum* cells in a logarithmic growth

phase are inactivated. Rahman et al does not disclose or suggest an inactivated vaccine, nor does this reference suggests any relationship between the virulence and the vaccine's efficacy, much less disclose that there is a higher effect of the vaccine which is made from a logarithmic phase culture. Instead, with Rahman et al in hand, the skilled artisan would be led to the conclusion that there is no difference between the efficacy of a vaccine made from a culture in logarithmic phase and one that is in a stationary phase.

In view of the foregoing, Applicants submit that the presently claimed invention is not anticipated by Rahman et al.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 1-2 under 35 U.S.C. §102(b) over Kondo et al (2001) is respectfully traversed.

The Examiner has also maintained the rejection over Kondo et al (2001). It is not clear why this rejection was maintained as the Examiner does not specifically address the deficiencies in this disclosure that were highlighted in Applicants prior response. Specifically, applicants again submit that Kondo et al (2001) merely discloses a 36-hour logarithmic growth phase culture. Amended Claims 1 and 2 require additional components (i.e., one or more pharmaceutically acceptable carriers or adjuvants). Apparently, the Examiner's position is that the presence of these components relates to an issue of purity but do not alter the product in any way. As such, the Examiner maintains that the product disclosed by Kondo et al (2001) anticipates the claimed invention.

However, it should be noted that Kondo et al (2001) suffers from at least one additional deficiency. Specifically, Kondo et al (2001) does not disclose or suggest an inactivated vaccine, nor suggests any relationship between the virulence and the vaccine's

efficacy. Vaccines currently used are made from both high virulent cells and low virulent cells. Therefore, it is unexpected based on the virulence of cells if the vaccine is effective or not and there is no disclosure or suggestion as to a correlation between virulence of cells and efficacy of the vaccine made from such a cell.

In view of the foregoing, Applicants submit that the presently claimed invention is not anticipated by Kondo et al (2001).

Applicants request withdrawal of these grounds of rejection.

The rejections of Claims 1-30 under 35 U.S.C. §102(a) or, in the alternative, under 35 U.S.C. §103(a) over Kondo et al (Diseases of Aquatic Organisms, 2003), are respectfully traversed on the ground that Kondo et al (Diseases of Aquatic Organisms, 2003) is not prior art against the present application.

Kondo et al (Diseases of Aquatic Organisms, 2003), was published on August 4, 2003. The present application is a National Stage (371) of PCT/JP03/16180 filed on December 17, 2003, which claims priority to JP 2002-366769 filed on December 18, 2002. To perfect their claim to foreign priority, Applicants **submit herewith** a certified English translation of JP 2002-366769. Applicants request that the Examiner acknowledge entitlement of the present application to the benefit of an earlier filing date provided by the claim to priority to JP 2002-366769, which is over 8 months prior to the publication of Kondo et al (Diseases of Aquatic Organisms, 2003). Since Kondo et al (Diseases of Aquatic Organisms, 2003) is not prior art against the present claims these rejections should be withdrawn.

Acknowledgment that these grounds of rejection have been withdrawn is requested.

The rejection of Claims 12-13 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Applicants have amended Claims 12 and 13 to address the Examiner's specific points of criticism.

In view of the amendments herein, Applicants request withdrawal of this ground of rejection.

Applicants submit that the application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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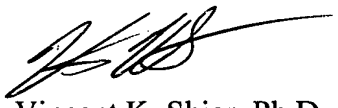

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